

Remarks

Claims 1-18 are canceled herein and replaced by new claims 19-37. Claims 19-37 are pending in the application. Applicants reserve the right to pursue the subject matter of original claims 1-18 in continuing applications.

Support for the negative selection marker and antibiotic resistance gene in new independent claim 19 is found, *inter alia*, throughout the specification and in Figure 11A. Support for the toxic genes in claims 24 and 25 is found, *inter alia*, throughout the specification and in paragraph [0124] on page 26 of the specification. Support for the antibiotic resistance genes of claim 26 is found, *inter alia*, throughout the specification and in Figure 2A. Support for the *att* site core regions in claim 31 is found, *inter alia*, throughout the specification and in paragraph [0182] on page 46. Therefore, new claims 19-37 do not add new matter.

I. Rejection of the Claims Under 35 U.S.C. § 102(b)

Claims 1-7 and 9-16 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Johnson *et al.* (WO 93/19172). (Office Action, page 2.) Claims 1-18 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Griffiths *et al.* (U.S. Patent No. 5,962,255). (Office Action, page 3.) Claims 1-8, 14, 17 and 18 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Griffiths *et al.* (U.S. Patent No. 6,010,884). (Office Action, page 4.) Applicants respectfully disagree with these rejections but have added new claims to facilitate prosecution.

Applicants also note that the Examiner has interpreted the the term “recombination site” to include restriction enzyme sites. (Office Action, page 4.) This interpretation of the term is not supported by the specification and is contrary to that used in the art. Paragraphs [0003] through [0005] on pages 1-2 of the specification describe site specific recombinases, also known as recombination proteins. These recombinases “recognize specific sequences of bases in DNA and exchange the DNA segments flanking those segments.” The specification further states in paragraph [0106], on page 21 that “[r]ecombinational cloning according to the present invention thus uses recombination proteins with recombinant nucleic acid molecules having at least one selected recombination site for moving or

exchanging segments of nucleic acid molecules, *in vitro* and *in vivo*.” Applicants assert that one skilled in the art, upon reading the specification, would not interpret the term “recombination site” to include restriction enzyme sites.

New independent claim 19 is directed in part to a method of cloning an amplification product by obtaining an amplification product “comprising, in order, a first recombination site, a product nucleic acid and a second recombination site,” and combining the amplification product with a vector “comprising, in order, a third recombination site, a negative selection marker, an antibiotic resistance gene and a fourth recombination site.”

In order to anticipate, a single reference must disclose “each and every limitation of the claimed invention.” (*Helifix Ltd. v. Blok-Lok, Ltd.*, 208, F.3d 1339, 1346 (Fed. Cir. 2000).) None of the cited references, teach the use of a negative selection marker in methods for cloning an amplification product as is recited in claim 19. Applicants therefore believe that new claims 19-37 are not anticipated by the cited references.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 102(b).

II. Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph

Claims 9, 11, and 13 stand rejected under 35 U.S.C. § 112, First Paragraph, for failing to comply with the written description requirement. (Office Action, page 5.) Applicants respectfully disagree but have added new claims to facilitate prosecution.

Claims 9, 11 and 13 are canceled herein and have been replaced by new claims 27, 29 and 32 directed to similar subject matter. These new claims refer only to *lox*, *att* or FRT recombination sites and do not recite functional mutants thereof.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 112, First Paragraph.

III. Rejection of the Claims Under 35 U.S.C. § 112, Second Paragraph

Claims 1-18, stand rejected under 35 U.S.C. § 112, Second Paragraph, for being indefinite and for failing to particularly point and distinctly claim the subject matter which the applicant regards as the invention. (Office Action, page 7.) In particular, the Examiner asserts that the term “in vitro” does not distinguish between inside of a cell in a culture

vessel and outside of a cell. The term “in vitro” has been replaced in new claim 19 with the phrase “outside of a cell” to more clearly define the scope of the invention.

The Examiner also asserts, that in claims 3-7 it is unclear which vector is being referred to. (Office Action, page 7.) New claims 21 and 22, which are directed to similar subject matter as claims 3-7, refer to the “product vector” to make it explicitly clear which vector is being referred to. In view of these remarks, Applicants believe that the Examiners concerns have been addressed by the new claims.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 112, Second Paragraph.

IV. Double Patenting

Claims 1, 4, 6-18 stand rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 29-34 of U.S. Patent No. 5,888,732. (Office Action, page 8.) Claims 1-18 stand rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 15-20 and 45-55 of U.S. Patent No. 6,720,140. (Office Action, page 9.)

Applicants defer responding to this rejection until patentable subject matter has been determined at which time Applicants will consider whether a terminal disclaimer is needed.

Claims 1-18 stand provisionally rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 52-59 and 61-67 of co-pending Application No. 10/680,316. (Office Action, page 9.)

Applicants point out that Application No. 10/680,316 is now abandoned, rendering this rejection moot.

Conclusion

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

/Peter G. Foiles/

Peter G. Foiles
Agent for Applicants
(240) 379-4173
Registration No. 46,477

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